

Application No. 10/824,321
Amendment dated June 8, 2006
After Final Office Action of April 10, 2006

6

Docket No.: 56369(70157)

REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application. Applicants request reconsideration of the subject application based on the instant amendments and following remarks.

Claims 38, 39, 41, 44, 46, 47, 49, and 55 have been amended. Claims 1-37, 40 and 50-54 have been cancelled without prejudice or disclaimer. Support for the instant amendments can be found in the claims as originally filed and throughout the specification. No new matter has been added by the claim amendments.

Claim 40 has been rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 40 has been cancelled by the instant amendment without prejudice or disclaimer.

Thus, the claims, as amended, are fully compliant with 35 U.S.C. 112, second paragraph, definiteness requirements.

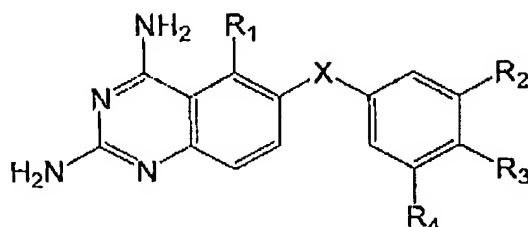
Claims 39-49 and 55 were rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Broughton et al. (Antimicrobial Agents and Chemotherapy, 1348-1355, 1991).

Application No. 10/824,321
Amendment dated June 8, 2006
After Final Office Action of April 10, 2006

7

Docket No.: 56369(70157)

The Broughton document teaches, in Table 8, a series of compounds of the structure:



Broughton recites six (6) compounds of the above-referenced structure. Five of the compounds have a methyleneamino X group, i.e., a -CH₂NH- residue linking the two aromatic groups. Only a single compound, 351521, has a methylene linker at the X position. Each of the compounds in Table 8 have an alkyl residue at the R₁ position.

The Examiner asserts that one of ordinary skill in the art would be motivated by the teaching of Broughton to make compounds of Table 8 in which the R₁ alkyl residue is replaced by a hydrogen because exchange of methyl and hydrogen residues is an obvious variation.

Applicants respectfully disagree. The entire teaching of Broughton would not motivate one of ordinary skill in the art to modify compound 351521 with the expectation of obtaining active compounds.

Broughton clearly teaches that compound 351521 is not a desirable compound for additional development. Not only does compound 351521 have the highest IC₅₀ value against *P. carinii* dihydrofolate reductase of the 5 compounds compared to trimetrexate in Table 8, but compound 351521 also has the lowest selectivity for *P. carinii* (RL/PC ratio is 0.047) of all the compounds in Table 8 including trimetrexate. Thus, one of ordinary skill in the art would not have been motivated from the Broughton disclosure to modify the 351521

Application No. 10/824,321
Amendment dated June 8, 2006
After Final Office Action of April 10, 2006

8

Docket No.: 56369(70157)

compound nor would one of ordinary skill in the art have a reasonable expectation that such a modification would provide *P. carinii* dihydrofolate reductase selective inhibitors.

Thus, the Broughton reference clearly teaches away from modification of the compounds recited in Table 8 and more particularly teaches away from modification of compound 351521. One of ordinary skill in the art would lack motivation to modify compound 351521 or a reasonable expectation of obtaining superior biological data by such a modification.

For instance, it is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the cited reference to make the claimed invention, nor is there a reasonable expectation of success.

Thus, claim 39, as amended, are patentable over Broughton. Claims 41-49 and 55 depend from claim 39, and are therefore also patentable over Broughton. Applicants respectfully request withdrawal of the rejections and reconsideration of the claims.

Application No. 10/824,321
Amendment dated June 8, 2006
After Final Office Action of April 10, 2006

9

Docket No.: 56369(70157)

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: June 8, 2006

Respectfully submitted,

By 

John B. Alexander, Ph.D.

Registration No.: 48,399

EDWARDS ANGELL PALMER & DODGE LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617) 439-4444

Attorneys/Agents For Applicant